Remarks

Upon entry of the foregoing amendments, claims 1-101 are pending in this application. Claims 12-51 and 63-101 have been withdrawn from consideration as being directed to a non-elected invention. Claims 6-7 and 57-58 have been cancelled. Applicant maintains the right to file one or more continuation or divisional applications on any canceled subject matter.

Objection to the Specification

The Examiner has objected to the use of trademark recitations in the instant specification. The use of the terms "STIMULON™", "QS-21™" and "MPL™" were not capitalized and accompanied by the generic terminology throughout the specification.

Applicant is hereby submitting a substitute specification and a marked up copy of the original specification that address this objection. Applicant submits that there is no new matter added to the substitute specification and respectfully requests a withdrawal of the objections.

Double Patenting Rejection

Claims 1, 8, 9, 52, 56, 59, 60 and 62 are rejected under non-statutory obviousness-type double patenting as allegedly being unpatentable over Claims 1, 10, 13, 14, 15, 24 and 25 of US Patent No. 7,384,640 in view of Agren et al., (J. Immunol. 1999. 162 (2): 2432-2440).

Applicant respectfully requests that these rejections be held in abeyance until patentable subject matter is determined.

Rejections under 35 U.S.C §112

Claims 52-62 stand rejected under 35 USC §112, Second Paragraph as allegedly being indefinite for failing to point out and distinctly claiming the subject matter of the invention.

The Examiner alleges that the preamble of the above mentioned claims are drawn to a method of immunizing a mammalian host, but that the recited steps within the method do not state what the host is immunized from. Applicant has amended Claim 52 to read:

"A method of immunizing a mammalian host against disorders associated with β-amyloid protein comprising administering to the host an immunogenic amount of a composition comprising a cholera holotoxin (CT and an Aβ 1-7 peptide antigen…".

Applicant believes that these amendments to claim 52 render the rejection under 35 USC §112, second paragraph moot and withdrawal of this rejection is respectfully requested.

Claim Rejections- 35 USC §103

Claims 1-11 and 52-62 are rejected under 35 USC §103 (a) as allegedly being unpatentable over Jobling et al., (WO 00/18434) in view of Agren et al., (J. Immunol. 1999, 162(2): 2432-2440, hereafter "Agren"). Applicant traverses this rejection.

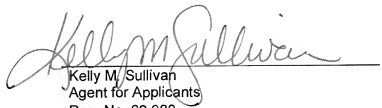
The present invention relates to a mutant cholera holotoxin which functions as both an adjuvant and an antigen carrier. An embodiment of the present invention is directed to a mutated cholera toxin (CT) that is genetically modified at residue 29 of the A subunit wherein the amino acid substitution is not an aspartic acid. In some embodiments the amino acid substitution at position 29 is a histidine (CT_{E29H}). In certain embodiments of the present invention the antigen is covalently associated with the CT_{E29H}. Throughout the Examples section of the present specification a number of different classes of antigens, including carbohydrate antigens, peptide antigens and lipooligosaccharide antigens were conjugated to mutant CT_{E29H} using various chemistries. In particular, conjugates were made with CT_{E29H} and the amino-terminal amino acids 1-7 of the 42 amino acid β-amyloid peptide. The results in the present specification show that mutant CT_{E29H} functions both as a carrier protein and as an adjuvant while maintaining intrinsic adjuvant properties. As shown in Examples 5-9, the CT_{E29H}/Aβ 1-7 show antigen-specific immune responses when animals were administered the conjugate, demonstrating that the conjugate is an effective carrier and adjuvant for the Aβ 1-7 peptide. Applicant has amended claims 1 and 52 to define the antigen as Aβ 1-7. In contrast, Agren teaches a gene fusion product of the A subunit of CT conjugated to a B-cell targeting moiety, DD (Ig binding fragment D of Staphylococcus aureus protein A). The DD portion of the CT-DD conjugate targets the conjugate to B cell and further adds to the adjuvanting properties of CT. Agren teaches an enhanced immune response to the conjugated adjuvants when co-administered with different antigens. Agren teaches combination of two adjuvants and the combination's enhanced ability to immunomodulate, while Applicant's claimed invention is a mutated CT covalently associated with an Aβ 1-7 antigen, not another adjuvant. Additionally, the DD portion of the CT-DD conjugate comprises two D subunits, each of which comprises 61 amino acids (122 amino acids in total). Applicant's invention comprises one peptide of 7 amino acids conjugated to the mutated CT. There are no teachings in Agren or Jobling that a peptide the size of 7 amino acids would be effective as a part of a conjugate when in contrast Agren teaches the use of 2 polypeptides overall having the size of 122 amino acids.

The Examiner has failed to prove a prima facie case of obviousness based on Jobling in view of Agren. The Examiner states on page 6 of the Office Action dated March 9, 2009 that it would have been prima facie obvious at the time of the applicant's invention to apply Agren's covalently associated cholera holotoxin with an antigen that target powerful bacterial enzymes. Agren does not, in fact, teach a covalently associated CT with an antigen, but a genetically constructed CT with another adjuvant, not an antigen. Additionally, neither Agren nor Jobling teach that a peptide the size of Applicant's claimed invention, amino acids 1-7 of the 42 amino acid β-amyloid peptide (Aβ 1-7), would work in a conjugate with the mutated CT. Agren teaches a polypeptide the size of 122 amino acids that help the mutated CT's adjuvanting properties when combined with antigens.

In light of the arguments presented herein Applicant respectfully submits that the rejection under 103(a) is improper and should be withdrawn.

Conclusion

In conclusion, this reply is believed to be a full response to the outstanding Office Action. Should any issues remain outstanding or if there are any questions concerning this paper, or the application in general, the Examiner is invited to telephone the undersigned representative at the Examiner's earliest convenience.



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